Re-educating immune system: New cell therapy prevents organ rejection

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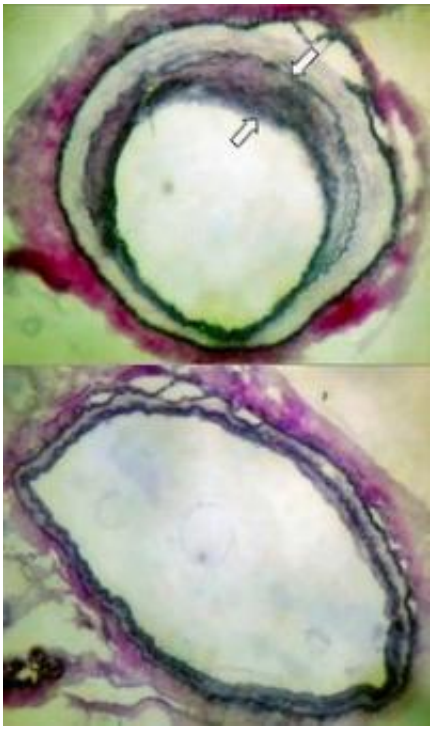

The rejection response (top, arrows) to a transplanted blood vessel in a mouse is prevented by an immune cell therapy (bottom). Image courtesy of Science/AAAS.

Researchers at King's College London have used cells found naturally in the body, to re-educate the immune system to prevent rejection of an organ transplant while remaining capable of fighting infections and cancer.

Currently, patients must take immunosuppressant drugs to prevent a new organ from being rejected after transplantation. However, these drugs suppress the entire immune system, leaving the patient susceptible to infections and tumours.

Scientists say this new approach using immune cells, called regulatory T cells (Tregs), from the body could eliminate the need for immunosuppression, as the Tregs used will only suppress the activity of those cells which will attack the new organ, rather than suppress the whole immune system. The team says these results are encouraging. Ultimately this approach could extend the life of a transplanted organ and in turn, could alleviate the organ shortage problem.

The study, to be published in *Science Translational Medicine*, was carried out at King's by scientists in its Medical Research Council Centre for Transplantation. King's College London is part of King's Health Partners Academic Health Sciences Centre, a pioneering collaboration with NHS Trusts which aims to ensure that the latest research in health is used to improve patient care at the earliest opportunity.

The study was part-funded by the British Heart Foundation and the Wellcome Trust.

Tregs are known to control the activity of many different immune cells, including T effector cells, which are responsible for mounting immune responses against foreign organisms, such as bacteria during an infection, and an organ following transplantation. The team have developed a method to select Tregs that can regulate only the activity of effector cells that would target a transplanted organ ("specific" Tregs), leaving the remaining effector cells to function normally.

Using a humanised mouse, where a mouse lacking its own immune system was given human effector cells and Tregs, the team were able to

test the ability of these "specific" Tregs to prevent rejection of human skin grafted onto the mouse. The team found that the "specific" Tregs were significantly more potent than non-specific Tregs (those able to inhibit all effector cells) in protecting skin grafts from immune damage.

Professor Robert Lechler, Vice-Principal for Health at King's and Executive Director of King's Health Partners, said: 'This study is a promising step forward that could lead to dramatic advances in preventing organ rejection and improving the quality of life of transplant patients.

'Researchers at King's are in a unique position. On average it takes 17 years for research discoveries and medical breakthroughs to become routine clinical practice. But being an Academic Health Sciences Centre means that researchers work directly alongside clinicians at leading NHS Foundation Trusts to speed up the time it takes for research to get from bench to bedside. Because of this, we hope to begin first-in-man trials within five years and could see patients being given this novel cellular therapy in around ten years time.'

If this approach were to be adopted to treat patients, blood would be sampled from a patient who will be receiving a transplant and their Tregs extracted from it. These Tregs would then be mixed with cells from the selected organ donor and the "specific" Tregs isolated using the new method developed by the team. The specific Tregs would then be expanded in numbers in a specialised sterile laboratory and be reintroduced into the patient after the transplant. Scientists believe this therapeutic approach will be applicable to the majority of solid organ transplants such as the kidney, heart and liver.

The King's study is one of three papers in Science Translational Medicine reporting progress towards immune cell therapies to prevent transplant rejection. Together, they make it possible to see how such

therapies might work, if successfully developed.

Provided by King's College London